# Letter in response to "A case of primary and secondary syphilis presenting together as immune reconstitution inflammatory syndrome"

Sir,

We read with interest the article entitled "A case of primary and secondary syphilis presenting together as immune reconstitution inflammatory syndrome (IRIS)" by Mitra *et al*.[1] The authors have presented the simultaneous occurrence of primary and secondary syphilis in a human immunodeficiency virus (HIV)-positive patient on antiretroviral therapy (ART) labeling this event as a part of IRIS.

Syphilis is a bacterial infection caused by *Treponema pallidum*, transmitted commonly through the sexual route. After a variable incubation period, it presents as a solitary painless ulcer with indurated base associated with inguinal lymphadenopathy. After 2–12 weeks of development of lesion of primary syphilis, the patient may develop features of secondary syphilis which include characteristic coppery-brown papules and plaques over various parts of the body including the palms and soles. In some patients, both primary chancre and lesions of secondary syphilis can be present simultaneously. IRIS is defined as the development of inflammatory or infectious disease in an HIV-positive patient with low CD4 count and high viral load who has been recently started on ART, and this process cannot be explained by the natural course of the newly acquired opportunistic infection, the natural course of the previously diagnosed opportunistic infection, or drug toxicity.[2]

The authors have labeled their patient as having primary and secondary syphilis as the manifestation of IRIS, but

we feel that it is just syphilis (primary and secondary) and HIV coinfection.

After 6 weeks of ART and azithromycin prophylaxis, the patient developed genital ulcer and lesions on the soles suggestive of secondary syphilis. Venereal disease research laboratory (VDRL) test was negative but the treponema pallidum hemagglutination, a specific treponemal test was highly positive in a dilution of 1:1024, confirming the diagnosis of syphilis. The presence of primary and secondary lesions together in the natural course of the disease is well-described in literature, both in HIV-infected and non-HIV-infected patients.[3-6]

However, there was no paradoxical worsening of the symptoms – as it is a must for considering a diagnosis of IRIS – which certainly cannot be considered in this case in any possible scenario.

Another important issue that needs attention is the continued prophylactic use of azithromycin and what effect it is expected to have on the establishment of treponemal infection and then the disease following its usual course – which again seems very unusual. Hence, the only way to explain the acquisition of syphilis and its continuation in a patient on regular intake of azithromycin is to assume that either the patient was not taking the drug or the serum levels of azithromycin were so low that it did not affect the course of syphilis, which is very difficult to presume – when treponemes are known to be highly sensitive to all antimicrobial therapies.

The authors have mentioned that after 6 weeks of ART, the HIV viral load was undetectable; however, the median time to achieve undetectable viral load in HIV patients after starting ART is 181 (range: 140–221) days.[7] Considering the very high initial viral load (300,000 copies/ml) and very low CD4 count (20 cells/μl), it would take a still longer time to suppress the viral load to below the detection level obviously, this observation needs to be confirmed.

VDRL has 100% sensitivity in secondary syphilis. The authors have mentioned the prozone phenomenon to be responsible for its negativity. It would have been prudent to repeat the VDRL test after dilution to bring antibody titer in zone of equivalence, because it is necessary to monitor the treatment response and consider treatment failure if the fall in the titer is insufficient. It is the responsibility of the clinician to inform the laboratory about the possibility of the prozone phenomenon when the clinical suspicion is so strong. Moreover, if in the unlikely situation of earlier immunosuppression affecting the VDRL test positivity, repetition of the VDRL test after the fall in the viral load would have given a better picture.

The biopsy was taken from the skin lesions on the sole which confirmed syphilis. It is most likely that the patient had acquired syphilis before attending the clinic and the diagnosis of HIV and secondary stage of syphilis were also present at the time of reporting. The ulcerative lesion on the penis may not be syphilitic and could be something else, as it is not fully investigated. However, whatever the real picture, there was no telescoping of primary and secondary syphilis as claimed.

The authors have mentioned "annular plaques over the soles," but the clinical picture shows discoid plaques. The clinical details provided by the authors about the index case are inadequate, particularly the gap between the development of primary chancre and the lesions on the soles, status of the lymph nodes, site of the biopsy, and special stains to demonstrate treponemes.

The authors have mentioned that the reason for false-negative VDRL or prozone phenomenon is due to antigen excess, but it is actually due to high antibody titer which inhibits agglutination.[8]

The authors have treated the patient with three doses of benzathine penicillin G, but the recommended dose for both primary and secondary syphilis is a single dose.[9,10] The reason for deviation from the recommended standard treatment protocol is not mentioned. Besides, some grammatical errors of language such as "cunts" instead of counts, "ignition" instead of initiation, "current" instead of currently, and "beyond" instead of before could have been avoided.

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**Conflicts of interest**
There are no conflicts of interest.

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